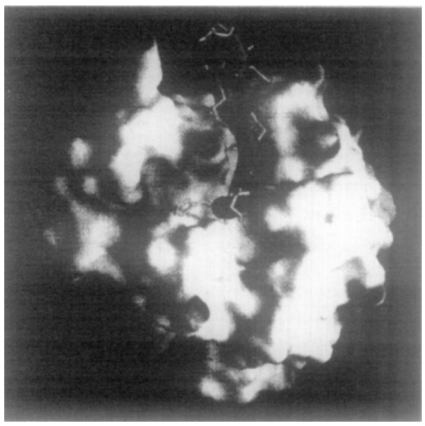
☐ **Cyclophilin A complexed with a fragment of HIV-1 gag protein: insights into HIV-1 infectious activity.** Yingdong Zhao, Yongquan Chen, Mike Schutkowski, Gunter Fischer and Hengming Ke (1997). *Structure* **5**, 139–146.

Cyclophilin A (CyPA), a receptor for the immunosuppressive drug cyclosporin A, catalyzes the *cis–trans* isomerization of peptidyl-prolyl bonds and is required for the infectious activity of human immunodeficiency virus type 1 (HIV-1). The crystal structure of CyPA complexed with a 25 amino acid peptide of HIV-1 gag capsid protein was determined at 1.8 Å resolution. The sequence Ala88–Gly89–Pro90–Ile91 of the gag fragment is the major portion of the peptide to bind to the active site of CyPA. Two residues of the 25-mer (Pro90–Ile91) bind to CyPA in a similar manner to two residues (Pro–Phe) of the CyPA substrate, succinyl-Ala–Ala–Pro–Phe–*p*-nitroanilide (AAPF). But the hydrogen-bonding pattern and molecular conformation of the amino terminus of the 25-mer (Ala88–Gly89) is different from that of AAPF. The peptidyl-prolyl bond between Gly89 and Pro90 of the 25-mer has a *trans* conformation, in contrast to the *cis* conformation observed in other known CyPA–peptide complexes. The residue preceding proline, Gly89, has an unfavorable backbone conformation that is not normally accessible to residues other than glycine, suggesting that binding between HIV-1 gag protein and CyPA requires the sequence Gly-Pro; the *cis–trans* activity, in contrast, appears to accept any amino acid before Pro. Thus, in HIV-1 infectivity, CyPA is likely to function as a chaperone, rather than as a *cis–trans* isomerase. But the similarities between the carboxyl termini of the 25-mer and the substrate AAPF mean that the involvement of the *cis–trans* isomerase activity of CyPA cannot be completely ruled out.



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